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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,684	02/27/2004	Alan L. Epstein	1920-325N1/09801297	9775

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/789,684	EPSTEIN ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS.from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,26 and 27* is/are pending in the application.

4a) Of the above claim(s) *6-19,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amended claims 1, 4-5 (12/21/2006), and claims 2-3 are under consideration by the Examiner.

Claims 6-19, 26-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Receipt of applicant's arguments and amendments filed on 12/21/2006 is acknowledged.

3. The following previous objections and rejections are withdrawn in light of applicants amendments filed on 12/21/2006:

(i) the objection to the specification;

(ii) the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6, 008,319.

4. Applicant's arguments with respect to claims 1-5 have been considered but are moot in view of the new ground(s) of rejection.

4. Applicant's arguments filed on 12/21/2006 have been fully considered and were persuasive in part. The issues remaining and new issues are restated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim rejections-35 USC § 112, first paragraph

6a. Claims 1-5, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons of record set forth at pages 3-4 of the previous Office action (8/23/2006).

Applicants argue that as amended claims 1-5 encompass a fragment of IL-2 containing an amino acid sequence corresponding to residues 37-58 of SEQ ID NO:3. However, contrary to Applicants arguments the claim 1 recites "comprising a fragment of IL-2". The written description in this case only sets forth vasoactive peptides consisting of amino acid residues 37-58 or 33-58 or 37-72 or 22-58 of SEQ ID NO:3, substantially free of IL-2 cytokine and therefore the written description is not commensurate in scope with the claims drawn to a vasoactive peptide comprising a fragment of IL-2. Amino acid sequences consisting of residues 37-58 or 33-58 or 37-72 or 22-58 of SEQ ID NO:3 meet the written description and enablement provisions of 35 U.S.C. 112, first paragraph. However, the indicated claims are directed to encompass homologues of the disclosed amino acid sequences having undisclosed amino acid sequences, which correspond to IL-2 sequences from other species. None of these amino acid sequences meet the written description provision of 35 USC 112, first paragraph.

Applicants argue that from the copy of the Bazan publication, Fig. 2, page 411, shows the alignment of the amino acid sequences of IL-2 from different animal species and that 50% (19/37) of the amino acid positions are identical within amino acids 22-58 of IL-2. However, The Cytokine Facts Book (1994), Robin Callard and Andy Gearing. Academic Press Inc. San Diego, CA, discloses that the amino acid sequence of IL-2 (interleukin-2) from human compared to mouse differs by 16 amino acids in length (page 39, table) and shares only about 60% identity (page 39, "Crossreactivity" section). Based solely on sequence, it would be clearly impossible for one skilled in the art to identify the mouse and human proteins as species homologues.

Furthermore, in the Bazan publication, Figure 2, helix A ranges from amino acid 12-28 and helix B ranges from 33-46. Therefore, contrary to Applicants arguments, Applicants have only described a vasoactive peptides 37-58 or 33-58 or 37-72 or 22-58 of SEQ ID NO:3 and have failed to provide a written description for other species.

6b. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated vasoactive peptide, said peptide consisting of residues 37-58 or 33-58 or 37-72 or 22-58 of amino acid sequence SEQ ID NO:3, substantially free of IL-2 cytokine activity, does not reasonably provide enablement for "all" vasoactive peptides which are fragments of IL-2 or a peptide consisting essentially of residues 37 to 58 of amino acid sequence SEQ ID NO:1 or a peptide consisting essentially of amino acid sequence SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 5-9 of the previous Office action (8/23/2006).

Applicants argue that together with the vasopermeability assays described in the specification and the knowledge in the art, peptides can be designed consisting of residues 27-58 of SEQ ID NO:3 without undue experimentation. However, contrary to Applicants arguments, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This position is consistent with the decisions in In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and Amgen Inc. V. Chugai

Pharmaceuticals Co. Ltd., 13 USPQ2d, 1737 (1990), and In re Wands, 8USPQ2d, 1400 (CAFC 1988) (which has been cited by Applicants. If Applicants will kindly review page 1404 of In re Wands, they will find that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims. Applicants arguments that the standard is that of making fragments or mutations in the IL-2 protein and testing to see if it retains the desired biological activity (in this case, enhancing vasopermeability) is a position that has been routinely dismissed by the courts, as shown by the decisions cited above.

Further, In re Wands determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally-occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing IL-2 peptides consisting essentially of residues 37-58 of SEQ ID NO:3 or residues 1-37 of SEQ ID NO:1. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed naturally-occurring IL-2 ligand sequence, which are required for functional and structural

integrity of the protein. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a the claimed peptides of IL-2 protein which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.

Furthermore, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph, in a recent CAFC decision, Genentech, Inc. v. Novo. Nordisk, 42 USPQ2d, 100 (CAFC 1997), in which the decisions in In re Fisher, Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., and In re Wands were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the Court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not, without actually making and testing them, then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that a peptide consisting essentially of residues 37-58 of SEQ ID NO:3 or residues 1-37 of SEQ ID NO:1 will more likely than not perform in the manner disclosed and the instant specification does not provide the guidance needed to predictably alter

these two sequences with any reasonable expectation that the resulting protein will have enhanced vascular permeability.

Claim rejections-35 USC § 112, second paragraph

7. Claims 1-5, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth at pages 9-10 of the previous Office action (8/23/2006).

Amended claim 1, line 2, is vague and indefinite because it recites "contains an amino acid sequence". It is suggested that the claim be amended to recite the conventional "comprises amino acid residues 37-58".

Claims 3-4, remain rejected as vague and indefinite for reciting "consisting essentially of" because the metes and bounds of the claims are unclear. It is unclear if the claimed peptides are 50% identical to residues 37-58 of SEQ ID NO:3 or 50% identical to residues 1-37 of SEQ ID NO:1, are the claimed peptides 75% identical to residues 37-58 of SEQ ID NO:3 or 75% identical to residues 1-37 of SEQ ID NO:1? Applicants argue that the amendments to claims 3-4 clarify the subject matter of the claims. However, contrary to Applicants arguments, the amendments to the claims fail to overcome the 35 USC 112, second paragraph rejection because the limitation "consisting essentially of" is vague and indefinite because it is unclear which amino acids claimed are essential and which are not. It is suggested that the term "consisting essentially of" be deleted from the claims to obviate this rejection.

Claims 2 and 5 remain rejected insofar as they depend on the above rejected claims for their limitations.

Conclusion

Claims 1-5 are rejected.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
January 17, 2007